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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/570,937	07/17/2006	David Morton	478.1076	8966

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EXAMINER	
LEA, CHRISTOPHER RAYMOND	
ART UNIT	PAPER NUMBER
1619	
MAIL DATE	DELIVERY MODE
12/31/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/570,937	MORTON ET AL.	
	Examiner	Art Unit	
	Christopher R. Lea	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,24,39-43,46-57 and 59-64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,24,39-43,46-57 and 59-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 March 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/8/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application is a 371 (national stage application) of PCT/GB04/03935.

Receipt of Amendments/Remarks filed on September 8, 2009, is acknowledged. In response to Non-final office action dated May 6, 2009, applicant amended claims, 23, 43, 46, 48, 50, 53, 59, & 60, canceled claims 31, 38, 44, 45, & 58, and added no new claims. Claims 23, 24, 39-43, 46-57, & 59-64 are pending. Claims 23, 24, 39-43, 46-57, & 59-64 are under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. All new rejections applied have been necessitated by applicant's amendment to the claims. They constitute the complete set presently being applied to the instant application.

Information Disclosure Statement

1. The information disclosure statement(s) (IDS) submitted on September 8, 2009, was filed after the mailing date of the first office action on the merits. The submission is in compliance with the provisions of 37 CFR 1.97 & 1.98. Accordingly, the information disclosure statement has been considered by the examiner.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 23, 24, 39-43, & 59-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tam et al. (US PreGrant Publication 2002/0161016).

Applicant claims

Applicant claims a method for treating premature ejaculation through the pulmonary inhalation of an antidepressant in the form of a dry powder.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Tam et al. teach, as a whole, administration of antidepressants to treat premature ejaculation.

Claim 23 & 61-64: Tam et al. teach a composition containing clomipramine in a form for pulmonary administration (example 5, paragraphs 92 & 94). The composition is administered to a subject to treat premature ejaculation (PE) (paragraphs 105 & 106, and claims 1 & 21). Tam et al. teach that the composition for treating PE may be a dry powder (paragraph 74).

As to the claimed onset of efficacy, where the claimed and prior art products are substantially identical in structure or composition, or are produced by substantially identical processes, a *prima facie* case of obviousness has been established. Further, The U.S. Patent Office is not equipped with analytical instruments to test prior art compositions for the infinite number of ways that a subsequent applicant may present previously unmeasured characteristics. When as here, the prior art appears to contain the exact same ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is properly shifted to applicant to show otherwise. Absent evidence to the contrary, the prior art composition must possess the claimed onset of efficacy, since it is substantially identical to the claimed composition (See MPEP § 2112.01).

Claim 24: As to the claimed side effect profile, where the claimed and prior art products are substantially identical in structure or composition, or are produced by substantially identical processes, a *prima facie* case of obviousness has been

established. Further, The U.S. Patent Office is not equipped with analytical instruments to test prior art compositions for the infinite number of ways that a subsequent applicant may present previously unmeasured characteristics. When as here, the prior art appears to contain the exact same ingredients and applicant's own disclosure supports the suitability of the prior art composition as the inventive composition component, the burden is properly shifted to applicant to show otherwise. Absent evidence to the contrary, the prior art composition must possess the claimed side effect profile, since it is substantially identical to the claimed composition (See MPEP § 2112.01).

Claim 39: Tam et al. teach that a single antidepressant or a combination of antidepressants can be administered in the composition (paragraph 44).

Claims 40-42: Tam et al. teach that other active agents (not antidepressants) can be administered in the composition (paragraphs 44-46). Tam et al. also teach that the other active agents will generally be one that is effective in treating PE (paragraph 44). Tam et al. specifically teach benzodiazepines as possible other active agents (paragraph 46).

Claims 43, 59, & 60: Tam et al. teach that the composition delivers 0.1-300 mg per dose (paragraph 78).Tam et al. teach a composition (example 5) that has an effective dose of 8.25-24.75 mg (2.5 g in 100mL, 0.33mL/compression, 1-3 compressions/dose, paragraphs 92-95).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the teachings of Tam et al. and the instant claims is that Tam et al. do not exemplify an embodiment that possesses the claimed limitations (dry powder inhalation form, two antidepressants, or second active agent).

Finding of *prima facie* obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to treat premature ejaculation with the composition of Tam et al. formulated as a dry powder for inhalation and produce the instant invention. The skilled artisan would have been motivated to formulate the composition as a dry powder because Tam et al. teach/suggest such an embodiment of the formulation.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to formulate a composition for treating PE with 2 antidepressants, a second active agent as taught by Tam et al. and produce the instant invention. The skilled artisan would have been motivated to formulate the compositions with 2 antidepressants, a second active agent because it is within purview of the skilled artisan to select a known material based on its suitability for its intended use. Reading a list and selecting a known compound to meet known requirements is no more ingenious than selecting the last piece to put in the last opening in a jig-saw puzzle (see MPEP § 2144.07).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in formulating a composition for treating PE as a dry powder for inhalation as taught by Tam et al. and

producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

6. Claims 46-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tam et al. as applied to claim 23 above, and further in view of Staniforth et al. (US PreGrant Publication 2003/0162835).

Applicant claims

Applicant claims a method for treating premature ejaculation through the pulmonary inhalation of clomipramine in the form of a dry powder.

Determination of the scope and content of the prior art (MPEP 2141.01)

Detailed discussion of the rejection of claim 23 and the teachings of Tam et al. appears above.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the teachings of Tam et al. and the instant claims is that Tam et al. do not specifically teach the claimed size limitations, excipients, and carrier particles. This deficiency in Tam et al. is cured by the teachings of Staniforth et al.

Staniforth et al. teach, as a whole, a method for making particles suitable for use in inhalable pharmaceutical compositions. Staniforth et al. teach making composite excipient particles for use in formulations for the local administration of agents including antidepressants (paragraph 48).

Claims 46 & 47: Staniforth et al. teach that the composite excipient particles have a mass median aerodynamic diameter of not more than 10 μm advantageously and not more than 5 μm preferably (paragraph 51).

Claims 48 & 49: Staniforth et al. teach that 90% by weight of the composite excipient particles have a diameter of less than 10 μm advantageously and less than 5 μm preferably (paragraph 51).

Claims 50 & 53: Staniforth et al. teach that the composite excipient particles comprise an excipient and an additive material (paragraph 51).

Claim 51: Staniforth et al. teach that the optimum amount of additive material will depend on chemical nature of the additive material and excipient (paragraph 24). Further, Staniforth et al. teach that additive material is preferably 2-20% based on the total weight of the additive material and excipient (paragraph 24). Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation (MPEP § 2144.05).

Claim 52: Staniforth et al. teach that leucine, magnesium stearate, lecithin, and sodium stearyl fumarate may be additive materials (paragraphs 33-36).

Claim 54: Staniforth et al. teach the inclusion of carrier particles in the composition (paragraph 54) and that the particles are of the size between 20 and 250 μm preferably (paragraph 55).

Finding of *prima facie* obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the methods for making an inhalable

pharmaceutical taught by Staniforth et al. to formulate a composition for use in the method taught by Tam et al. and produce the instant invention. The skilled artisan would have been motivated to combine the teaching of the references because it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, namely for inhalation administration of an antidepressant, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (See In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) and MPEP § 2144.06).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in using the methods for making an inhalable pharmaceutical taught by Staniforth et al. to formulate a composition for use in the method taught by Tam et al. and producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

7. Claims 55-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tam et al. as applied to claim 23 above, and further in view of Lewis et al. (US PreGrant Publication 2002/0025299).

Applicant claims

Applicant claims a method for treating premature ejaculation through the pulmonary inhalation of clomipramine in a form useful in a pressurized metered dose inhaler.

Determination of the scope and content of the prior art (MPEP 2141.01)

Detailed discussion of the rejection of claim 23 and the teachings of Tam et al. appears above.

Claims 55-57: Tam et al. teach that the formulations for inhalation may be in the form of aqueous solutions and/or suspensions (paragraph 74).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the teachings of Tam et al. and the instant claims is that Tam et al. do not teach using the composition in a pressurized metered dose inhaler. This deficiency in Tam et al. is cured by the teachings of Lewis et al.

Lewis et al. teach, as a whole, stable pharmaceutical compositions for administration in a pressurized metered dose inhaler. Lewis et al. teach that the compositions may be used to administer active agents besides those specifically disclosed (paragraph 24).

Claim 55: Lewis et al. teach a composition comprising a solution of co-solvent and propellant in a pMDI (paragraph 16).

Claim 56: Lewis et al. teach that formulations for use in a pMDI can be a suspension, though this has been problematic (paragraph 4)

Claim 57: Lewis et al. teach that the propellants for use in the composition are HFAs, specifically HFA 134a and HFA 227 (paragraph 8).

Finding of *prima facie* obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the composition useful as an inhalable pharmaceutical taught by Lewis et al. to formulate a composition for use in the method taught by Tam et al. and produce the instant invention. The skilled artisan would have been motivated to combine the teaching of the references because it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, namely for inhalation administration of an active agent, in order to form a third composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art (See In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) and MPEP § 2144.06).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in using the composition useful as an inhalable pharmaceutical taught by Lewis et al. to formulate a composition for use in the method taught by Tam et al. and producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

In light of the forgoing discussion, one of ordinary skill in the art would have concluded that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Response to Arguments

8. Applicant's arguments filed September 8, 2009, have been fully considered but they are not persuasive.

Applicant argues that one of ordinary skill in the art would not be motivated to select a dry powder of clomipramine for treating PE from the teachings of Tam et al. because Tam et al. teach no benefit from choosing to make a dry powder for inhalation. The examiner disagrees in that Tam et al. clearly teach the embodiment of a dry powder for inhalation (even if it is not exemplified). No perceived benefit is necessary in light of this strong teaching/suggestion to make dry powder dosage forms of clomipramine for treating PE by inhalation. Applicant further argues that even if the skilled artisan were motivated to make a dry powder of clomipramine for inhalation treatment of PE from the teachings of Tam et al., Tam et al. does not disclose that the composition "provides an on set of the therapeutic effect within no more than 30 minutes following pulmonary administration". As stated above, since Tam et al. and the claimed invention are made of the same components (drug) and administered via the same route, they must possess this same property. Applicant has provided no evidence that the method of Tam et al. would not provide such an onset of symptoms. Applicant is reminded that any

such factually-supported objective evidence must be in affidavit/declaration form to be considered.

Applicant's arguments against Staniforth et al. and Lewis et al. focus on each reference individually. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Further, the examiner has laid out specific motivations to combine these references with Tam et al. Applicant has not pointed out any alleged errors in the examiner's reasons for combining, instead making unconvincing and general allegations that they may not be combined with Tam et al.

The expected result remains the same; an inhalable dry-powder composition of clomipramine for treating premature ejaculation is made in the absence of evidence to the contrary. No unexpected results have been presented. Applicant's arguments are not persuasive, and the rejection under 35 U.S.C. §103(a) is maintained.

Conclusion

Claims 23, 24, 39-43, 46-57, & 59-64 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher R. Lea whose telephone number is (571) 270-5870. The examiner can normally be reached on Mon-Fri 8:00-4:00 ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne "Bonnie" Eyler can be reached on (571)272-0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CRL

/Ernst V Arnold/

Primary Examiner, Art Unit 1616